

## Claims

I claim:

1. A hybrid fusion polypeptide, comprising:
  - (a) a multivalent portion that comprises at least two immunogenic amino-terminal polypeptides of Group A streptococcal M protein from at least two different Group A streptococcal serotypes; and
  - (b) a carboxy-terminal reiterated immunogenic polypeptide, which is carboxy-terminal to the multivalent portion and is a reiteration of a polypeptide from the amino-terminal region of the multivalent portion.
2. The hybrid fusion polypeptide according to claim 1 wherein at least one of said immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype selected from the group consisting of 1, 2, 3, 4, 5, 6, 11, 12, 13, 14, 18, 19, 22, 24, 28, 30, 48, 49, 52, and 56.
3. The hybrid fusion polypeptide according to claim 1 wherein the multivalent immunogenic portion of the fusion polypeptide consists of six immunogenic amino-terminal polypeptides of Group A streptococcal M protein from six different Group A streptococcal serotypes.
4. The hybrid fusion polypeptide according to claim 3 wherein the six different Group A streptococcal serotypes are 1, 3, 5, 6, 19, and 24.
5. The hybrid fusion polypeptide according to claim 1 wherein the multivalent portion of the fusion polypeptide consists of ten immunogenic amino-terminal polypeptides of Group A streptococcal M protein from ten different Group A streptococcal serotypes.

6. The hybrid fusion polypeptide according to claim 5 wherein the ten different Group A streptococcal serotypes are 1, 3, 5, 6, 18, 19, 22, 24, 28, and 30.

7. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 1.

8. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 2.

9. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 11.

10. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 13.

11. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 19.

12. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 22.

13. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein at least one of the immunogenic amino-terminal polypeptides of the fusion polypeptide is from a Group A streptococcal serotype 28.

14. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein the hybrid fusion polypeptide elicits an immune response comprising opsonic antibodies against Group A streptococcal M protein that do not cross-react with human tissue.

15. The hybrid fusion polypeptide according to claim 1 further comprising a marker encoded by an expression vector.

16. The hybrid fusion polypeptide according to claim 15 wherein the marker encoded by the expression vector is a His-tag.

17. The hybrid fusion polypeptide according to claim 15 wherein the encoded marker binds to nickel resin.

18. The hybrid fusion polypeptide according to any one of claims 1 to 3 wherein the immunogenic polypeptides of the fusion polypeptide are joined by amino acids specified by a restriction enzyme site.

19. The hybrid fusion polypeptide according to any one of claims 1 to 3 further formulated with an adjuvant.

20. The hybrid fusion polypeptide according to claim 19 wherein the adjuvant is alum.

21. The hybrid fusion polypeptide according to claim 19 further formulated with an immunomodulatory cofactor.

22. A composition comprising a hybrid fusion polypeptide according to any one of claims 1 to 3, and a pharmaceutically acceptable excipient, carrier, stabilizer or diluent.

23. The composition according to claim 22 further comprising with an adjuvant.

24. The composition according to claim 23 wherein the adjuvant is alum.

25. The composition according to claim 22 wherein the pharmaceutically acceptable excipient, carrier, stabilizer or diluent comprises at least one of a buffer, antioxidant, carbohydrate, and chelating agent.

26. The fusion polypeptide according to claim 22 wherein the composition further comprises an immunomodulatory cofactor.

27. The fusion polypeptide according to claim 26 wherein the immunomodulatory cofactor is selected from the group consisting of IL-4, IL-10,  $\gamma$ -IFN, IL-2, IL-12, and IL-15.